test for syphilis either in a negative or a positive sense. It is probable, however, that a combination of these two tests could be used, without any other aids, as a rapid means of excluding syphilis, because the false negatives of each would be revealed by the other. Excluding the separation and inactivation of the serums 144 specimens can be examined from beginning to end by one person in one-half to three-quarters of an hour. It has been stated that the antigen keeps well. This opinion is based on a comparison of the results with those of the Wassermann and Kahn reactions with antigens of different age, and on the results of a series of twenty-two picked serums which gave exactly the same results with a three months' old and a two days' old antigen.

Summary

(1) A modification of the Laughlen reaction using buffered saline is described.

(2) The method of preparation and use of the antigen is detailed.

(3) A comparison of the modified Laughlen, Wassermann and Kahn reactions on 2,104 serums is tabulated.

(4) The advantages of the use of this test as a sensitive screen are discussed.

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CORRESPONDENCE

GONOCOCCAL FIXATION TEST

Sir,—In Dr. Harkness's article entitled 'Drug Resistance in Gonorrhoea', I note he makes the following statement '. . . indeed a positive reaction (G.C.F.T.) is useless as a test of cure'. I presume that what he means is that if, during a test of cure, the G.C.F.T. is found to be positive, it is of no significance.

If this be true, it limits the value of this test considerably, and therefore it behoves Dr. Harkness to produce concrete evidence in support of his contention.

If, on the other hand, his contention is merely a pious hope based on intuition, and useful as a means of disregarding, Nelson-wise, an inconveniently positive G.C.F.T., it seems a pity that he should ever have given voice, in no uncertain way, to such an opinion. It can but lead astray the unwary and do much harm in making confusion worse confounded in the minds of the many for whom some are striving to evolve a reasonable test of cure for gonorrhoea.

London, W.1 I. N. ORPWOOD PRICE

Sir,—In his letter which appears above, Dr. I. N. Orpwood Price paraphrases a statement of mine on the gonococcal fixation test (G.C.F.T.) that if, during a test for cure, the G.C.F.T. is found to be positive, it is of no significance. He goes on to challenge me to produce concrete evidence in support of this contention. Here it is.

For many years this test has been carried out on all my patients suffering from venereal diseases, and during the last seven years Dr. Price himself has performed them on the majority of my private patients and on a small number attending me at hospital. My experience, therefore, extends over a number of years and if I were asked to discard one test, clinical or pathological, used in any stage of the disease, I should have no hesitation in saying that it would be the complement fixation test.

It is generally agreed that the complement fixation reaction for gonorrhoea registers the presence or absence of specific antibodies, but does not signify the presence or absence of gonococci in the tissues. It is interesting to note that in 1935 Dr. Price was maintaining that a positive test, provided no vaccine had been administered, was *always* indicative of the presence of living gonococci in the tissues, but that in 1938 he was not quite so dogmatic and considered that it was *almost always* the case.

This test, depending as it does on circulating antibodies, has become even more meaningless since the advent of sulphonamide therapy, which effects a rapid cure in a large majority of cases. Chemotherapy (in adequate dosage) prescribed early in the disease usually cures the infection before the blood becomes positive and the blood remains negative throughout the period of observation; but in the cases in which treatment is delayed for a week or longer it often becomes positive, and the longer the delay the more likely is it to remain positive after a cure has been effected. The clinician's only difficulties are in the small percentage of failures which are invariably occasioned by drug resistance, associated very rarely with closed foci of infection. In my experience negative results are always obtained when the resistance is 'partial' and often (and this may be

so even in cases suffering from arthritis) when the resistance is 'complete'. In the latter condition a positive reaction occurs more frequently after non-specific protein therapy, which may therefore stimulate the formation of large amounts of specific antibodies.

Dr. Price, in his monograph on the subject, states that it is useless to perform a test for cure until this test has become negative, but he overlooks the fact that gonococcal antibodies, when once formed, may persist for months, years or throughout life and that it is not necessary for an infective focus to co-exist. This is one of the chief reasons why I consider that a positive reaction is useless as a test for cure.

I have already published the results of this test, carried out on sixty stricture cases, attending for dilatations at the out-patient clinics at St. Peter's Hospital. The patients were between the ages of fifty-five and seventy years and the most recent gonococcal infection was of thirty-five years' standing. In 33 per cent there were positive reactions, but in no case were gonococci detected in the urinary tract. Furthermore, I have been consulted repeatedly by patients with positive serum reactions, who have previously attended elsewhere (sometimes for years of instrumentation combined with prostatic and vesicular massage) and have been refused a clean bill of health for marriage. I know that in a small percentage of these cases (when an all-night specimen of urine is clear with no threads, and smears after prostatic and vesicular massage are normal) Dr. Price has succeeded in growing organisms which give a positive oxidase reaction, but it has never been possible to grow these in pure culture, and in my opinion, derived from the overwhelming evidence of the other tests and subsequent observations, they are not gonococci.

In view of the frequency of persistent positive reactions which have no clinical significance, it is my considered opinion that physicians and surgeons should not rely upon this test in the diagnosis of suspected gonococcal complications, as its use frequently results in unnecessary mental agony to patients. A girl aged twenty-two years, serving in the Forces, was recently sent to me for an opinion. She had been diagnosed as suffering from rheumatic fever but, unfortunately for her, the G.C.F.T. showed a weak positive reaction. This was easily accounted for, when it was noted that the previous history showed an attack of vulvo-vaginitis at four years of age, persisting for some years in spite of treatment, during which period large numbers of antibodies would have appeared in the blood stream. The Service medical officers, however, while admitting that the hymen was intact and that gonococci had never been found in smears or cultures of the secretions, nevertheless labelled her, on the serum reaction only, as suffering from gonococcal arthritis. I wrote to the senior venereal diseases officer of the Service concerned and the word "gonococcal" has now been deleted from her documents.

The test is frequently negative when gonococci are present in the secretions and Dr. Price has ingenious explanations—'closed' and 'open' infections—for these discrepancies. He admits, however, that this state of affairs may exist in early infections of less than twenty-one days' duration, in infections limited to the anterior urethra in the male or the lower genitalia in the female and in infections of the vesiculae seminales and prostate which have been treated by massage; but he does not mention the only important group, those who are suffering from drug resistance. It is my considered opinion that infections in the male are never limited to the anterior urethra and that the posterior urethra is involved even during the incubation period of the disease. The test invariably gives negative results in ano-rectal infections in the male, and in a series of 110 cases it was positive on eight occasions only and two of these cases gave a previous history of gonococcal urethritis; the remaining six may very well have been false positives.

False positive reactions are indeed frequent in this test. Jacoby, Wishengrad and Koopman found non-specific reactions to be 15·5 per cent and Carpenter, in one of his series, found it as high as 71 per cent. There may also be cross-fixation with other allied organisms—Dr. Price admits that this may occur with *M. catarrhalis*.

There are many pitfalls in diagnosing gonorrhoea on weakly positive results and the following is an excellent example. In the pre-chemotherapy era a doctor's wife was transferred to me by a gynaecologist for the investigation of a vaginal discharge. Smears and cultures were negative for gonococci, but Dr. Price found the G.C.F.T. to be weakly positive. The test was repeated by five pathologists, including Dr. Price, who was the only one to return a positve reaction. In his report he stated that 'a weakly positive reaction (±) complement fixation reaction for gonorrhoea is, in my opinion, definite evidence of infection'. No gonococci, however, were found after repeated examinations.

The complement fixation test for gonorrhoea will, I feel certain, have the same fate as did a similar test for pulmonary tuberculosis.

London, W.1 A. H. HARKNESS

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Acute encephalopathy during neoarsphenamine treatment

Major W. A. Young in a personal communication refers to the article written by himself and Major S. Gordon which was published under the above title in the *Journal* for March, 1944. He states that a possible explanation of the large incidence of acute arsenical encephalopathy dealt with in the article was the fact that the arsenical solutions were sometimes allowed to stand for an hour before they were used.